PART IV

METABOLIC STUDIES
i) Iron and Anaemia
Chairman: Dr W Dukker
Iron Absorption in Chronic Renal Failure

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Anaemia in chronic renal failure is usually described as being normocytic, normochromic in the absence of blood loss. With the use of regular haemodialysis loss of blood into the dialyser is an introduced factor. Blood loss is liable to complicate the anaemia of chronic renal failure by the introduction of total body iron deficiency.

The aetiology of the anaemia of chronic renal failure not associated with blood loss is complex. The factors usually considered, upon which there is ample literature, include loss of erythropoietin from parenchymal destruction of the kidney. The red cell life is shortened, which phenomenon has been directly related to the level of the blood urea independently of the glomerular filtration rate (Shaw, 1967). Toxic suppression of the bone marrow by azotaemic plasma (Forsstrom, 1968) which may be indicated by paucity of reticuloocyte response (Shaw & Scholes, 1967) is a third factor described.

There seems to be a tacit assumption that there is a relative inability to absorb iron from the gastro-intestinal tract by patients with chronic renal failure. This facet does not appear to have been specifically documented, and has been explored in the present work.

MATERIALS AND METHODS

Eleven patients with chronic renal failure were examined. The majority of these were not in need of regular haemodialysis, and none were receiving peritoneal dialysis. The control group of 13 subjects were patients convalescent from acute non-renal illness and healthy members of staff. There was one control subject each suffering from malabsorption syndrome, gastro-intestinal bleeding due to aspirin toxicity, and post-gastrectomy iron deficiency. The remainder were all convalescent from acute myocardial infarction. These subjects having had explained to them the nature of the problem, and the means to be employed to investigate it, were told that the tests were entirely divorced from their own illness and treatment, and would contribute
nothing to their welfare. At this stage they were asked if they would care to participate.

Blood was drawn for measurement of the haemoglobin level, the serum iron, iron binding capacity and percentage saturation. The morphology of the blood film was noted. The blood urea, electrolytes and creatinine were measured. Bone marrow examination, by sternal puncture, was undertaken and note taken of the morphology and activity of the marrow, and in particular, the presence and degree of repletion of stainable iron stores.

Using 200 mg of ferrous sulphate in 100 ml of water as carrier, 10 μCi of $^{59}$Fe was administered by mouth after an overnight fast. Food was not permitted for a further one hour after the administration of the iron. Whole body counting using a shielded 5 inch (13 cm) diameter by 2 inch (5 cm) thick NaI (TI) crystal was undertaken on the day of receiving the isotope and on the 3rd, 7th, 10th and 14th day thereafter. The ratio of the count on the 14th day to that of the initial count was taken as the fraction (percentage) of the dose absorbed, according to the recommendation of Schiffer and his colleagues (1964) and Deller (1965).

![Graph](image)

**Figure 1.** Comparison of percentage of a dose of $^{59}$Fe absorbed by unselected group of control subjects and patients with chronic renal failure (C.R.F.)

Mean absorption, C.R.F. = 10.3%
Controls = 20.8%
RESULTS

It has been more difficult to present results than was anticipated. This arose from the high number of subjects without chronic renal failure who were found to have unsaturated iron stores in the bone marrow. Figure 1 presents the crude comparison of the percentage absorption of $^{59}\text{Fe}$ between patients with chronic renal failure and control subjects. It was felt that a more comparable appreciation of the situation would be reached by contrasting the $^{59}\text{Fe}$ absorption of subjects with a comparable state of iron repletion. A definition of iron deficiency has been reached, therefore, for the purposes of the present communication. It is: those subjects who show either frank hypochromic anaemia and/or frank iron deficiency in the bone marrow. Those subjects in whom the bone marrow report shows either normal iron stores or slight depletion, have been regarded as having normal bone marrow for the present purposes.

By the above criteria, the grouping resolves into 9 patients in group I.

![Figure 2. Comparison of percentage of a dose of $^{59}\text{Fe}$ absorbed by matched groups of control subjects with patients suffering from uncomplicated renal failure, and evidence of iron deficiency.](image)

- Gp. III, control subjects with replete body iron stores
- Gp. II, control subjects with depleted body iron stores
- Gp. I, patients with C.R.F. with depleted body iron stores

Mean absorption, Gp. I = 8.9%
Gp. II = 33.8%
Gp. III = 5.7%
with chronic renal failure, with unequivocal evidence of iron store depletion uncomplicated by other haematological disease. Two subjects with chronic renal failure had normal bone marrow iron stores, and are omitted from the grouping. Group II consists of 7 control subjects with unequivocally depleted iron stores, with or without peripheral evidence of anaemia, whilst the third group of control subjects had replete marrow iron stores, although one of these had a hypochromic film and a serum iron of only 55 μg/100 ml.

The most valuable comparisons can be drawn between the control subjects with iron store depletion and the patients with chronic renal failure, i.e. between group I and group II. The comparison of the $^{59}$Fe absorption between the 3 groups is shown in Figure 2. The mean percentage absorption of $^{59}$Fe for the controls with iron depletion was 33.8%, and the mean absorption for the patients with chronic renal failure was 8.8%. In the controls with replete iron stores, mean uptake of $^{59}$Fe was 5.7%.

No firm relationship could be seen at this stage between the serum iron or any other parameter that was measured, and the percentage absorption of $^{59}$Fe.

**DISCUSSION**

It is known that the avidity of gastro-intestinal absorption of iron is inversely related to body iron stores, and directly to the utilisation of iron in erythropoiesis (Deller, 1965). The absorption of iron is dependent upon the form in which it is offered to the gut (Pitcher et al., 1965; Williams, 1968) and it is acknowledged that greater absolute absorption of iron will occur when it is offered as food material than when offered as inorganic salts, as in the present work.

It was necessary to estimate the degree of repletion of body iron stores in order to assess the effect of this factor upon absorption. It is recognised that peripheral blood parameters (haemoglobin level, film morphology and serum iron levels etc) are late and unreliable indices of iron deficiency (Williams, 1968) and that liver and bone marrow stores indicate earlier stages of body iron depletion. By these criteria all the patients except two were found to have iron deficiency, and fortuitously half of the controls also had diminished marrow iron stores. This has in fact made two groups which are more directly comparable, but has not allowed us to establish a 'normal' range of iron absorption by this method, although others have published such data (Price et al., 1962). The common marrow deficiency of iron in our patients was in contra-distinction to the experiences of Wright et al (1968) whose untransfused patients had saturated iron stores. Kaye (1969) found that iron deficient patients had $^{59}$Fe absorption comparable to iron replete uraemics, but does not define iron deficiency for his patients. The advantage of parenterally administered iron over oral therapy as a haematinic is reflected in
several workers' experience (de Palma, 1969; Platts, 1969; Hawkins, 1970). Hawkins has indicated in a personal communication that, owing to repeated transfusions, many of his patients were probably iron replete.

It may well be that the depression of marrow activity believed to occur in azotaemia induces a poor utilisation of iron and that lack of utilisation dictates the poor uptake of iron. Whilst it has been suggested that this may be the most potent factor governing iron uptake by the gut (Deller, 1965), it is clear that these iron deficient patients have a low uptake compared with comparably deficient non-azotaemic patients.

The amount of data present is insufficient to permit correlation within the present study of the degree of iron absorption with any other factor which has presently been measured.

SUMMARY AND CONCLUSION

The present paper has presented data on the percentage absorption of a dose of $^{59}$Fe in patients with chronic renal failure exhibiting evidence of deficient iron stores, and a group of patients without renal disease also exhibiting evidence of deficiency of body iron stores. It is shown that there is evidence of a defect in iron absorption from the gut in chronic renal failure, compared to a control group of subjects without renal failure.

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